Preface

This book is intended to provide an introduction to human molecular genetics that is more focused and up to date than that found in large, general textbooks on genetics, and yet remains accessible to second and third year science undergraduates, medical students and other healthcare specialists. It assumes the background knowledge of genetics and molecular biology that would normally be taught in the first year of a university course. Not only is this a necessity to keep both the size and cost down, but it also seems futile to duplicate the coverage in the generous selection of excellent general textbooks to which most readers will have access. Each chapter ends with a list of further reading for those who would like to investigate a topic in more detail. For the most part the references are also the sources for most of the material presented in the chapter.

An introductory text to such a large and complex field must restrict itself to illustrating general principles with selected examples. Inevitably, work on many important genes must be omitted, and we can only apologise to those who feel their favourite gene has not received the attention it deserves. Equally, a certain amount of simplification is essential to make the content accessible to an undergraduate audience. This is particularly true of those areas such as population genetics and epidemiological genetics that are mathematically based, which experience shows can be a cause of difficulty to biology students. We can only hope that we have succeeded in spreading enlightenment without oversimplifying.

Since the second edition of this book was completed in 2001, the sequence of the human genome has been finished to a high standard and the difficult task of annotation is now essentially complete. Chapter 4 has been re-written to give an account of the finished genome sequence and the exciting new horizons and technologies that have opened up as a result. The latest innovation in sequencing has been the development of a new generation of sequencing technologies that promises to allow the rapid and

inexpensive sequencing of whole genomes and an account of these new methods is provided. In 2001, it was just becoming evident that the haplotype diversity of the human genome was less than expected. Subsequently, this observation has been exploited, along with the powerful new microarray technologies to allow the whole genomes to be scanned in populations of individuals to identify alleles that are associated with complex disease. These so-called 'genome wide association studies' have identified large numbers of risk alleles, and Chapter 6 has been completely rewritten to give an account of these developments. For the first time in this problematic field the positive findings have been consistently reproduced in independent studies. However, the combined risk of the alleles identified accounts for only a small part of the overall genetic variability observed in populations. The next development in this field is likely to be sequencing of whole genomes on a population-wide scale to allow the association of rare alleles to be tested. Such alleles are not captured by the microarrays currently used, which are limited by their design to genotype only those alleles that are relatively common. Since 2001, the use of siRNA as an experimental tool to silence human gene expression has developed from nowhere to become a powerful and much-used tool in human genetics. A new chapter has been added to give an account of siRNA and its applications.

The science of human molecular genetics develops at an ever-increasing pace, powered by the elucidation of the human genome sequence and the powerful new technologies that have developed to exploit this knowledge. The pace of these developments has made the objective of maintaining an up-to-date text increasingly difficult – major developments were transforming many fields even as we were writing. The 'data freeze' was applied at the end of August 2008.

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